

AMENDMENTS

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Claim 1. (Currently amended) A monomer polypeptide construct comprising at least one tetranection trimerising structural element (TTSE) which is covalently linked to at least one heterologous moiety, said TTSE being capable of forming a stable triple alpha helical coiled coil complex with two other TTSEs, wherein said complex remains as a trimer at a temperature of at least 60°C, and where the heterologous moiety is different from any of the fusion proteins CIIH6FXTN123, H6FXTN123, H6FXTN12, H6FCTN23, the sequences of which are shown in SEQ ID NOS:24-27.

Claims 2-18. (Canceled)

Claim 19. (Previously presented) An oligomer comprising at least two monomer polypeptide constructs according to claim 1.

Claims 20-21. (Canceled)

Claim 22. (Previously presented) A trimeric polypeptide complex according to claim 68, wherein the at least one heterologous moiety positioned N-terminally to a TTSE and the at least one heterologous moiety positioned C-terminally to a TTSE are part of the same monomer polypeptide.

Claim 23. (Previously presented) A trimeric polypeptide complex according to claim 68, wherein the at least one heterologous moiety positioned N-terminally to a TTSE and the at least one heterologous moiety positioned C-terminally to a TTSE are part of two separate monomer polypeptides.

Claims 24-67. (Canceled)

Claim 68. (Currently amended) A trimeric polypeptide complex comprising three monomer polypeptides, wherein (i) each of said monomer polypeptides comprises a tetranectin trimerising structural element (TTSE), said TTSE being a polypeptide having at least 68% amino acid sequence identity with the consensus sequence shown in Fig. 2, and (ii) at least one of said monomer polypeptides is covalently linked to at least one heterologous moiety, where said at least one heterologous moiety is different from any of the fusion proteins CIIH6FXTN123, H6FXTN123, H6FXTN12, H6FCTN23, the sequences of which are shown in SEQ ID NOs:24-27, and said complex remains as a trimer at a temperature of at least 60°C.

Claim 69. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein the sequence identity with the consensus sequence is at least 75%.

Claim 70. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein the sequence identity with the consensus sequence is at least 81%.

Claim 71. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein the sequence identity with the consensus sequence is at least 87%.

Claim 72. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein the sequence identity with the consensus sequence is at least 92%.

Claim 73. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein the TTSE comprises the consensus sequence shown in Figure 2.

Claim 74. (Previously presented) The trimeric polypeptide complex according to claim 1, wherein the TTSE is derived from human tetranectin, murine tetranectin, C-type lectin of bovine cartilage, or C-type lectin of shark cartilage.

Claim 75. (Previously presented) The trimeric polypeptide complex according to claim 74, wherein the TTSE is derived from human tetranectin and comprises the amino acid residues V17 to V49 (exon 2) shown in Figure 1.

Claim 76. (Previously presented) The trimeric polypeptide complex according to claim 75, wherein the TTSE derived from human tetranectin further comprises the amino acid residues C50 to K52 of exon 3 as shown in Figure 1.

Claim 77. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein the monomer polypeptides further comprises the amino acid residues E1 to D16 (exon 1) shown in Figure 1.

Claim 78. (Previously presented) The trimeric polypeptide complex according to claim 75, wherein at least one amino acid residue of exon 2 selected from the group consisting of amino acid residue nos. 21, 22, 24, 25, 27, 28, 31, 32, 35, 39, 41, 42, is/are substituted by any non-helix breaking amino acid residue, the amino acid residue numbering referring to amino acid residues in SEQ ID NO:7.

Claim 79. (Previously presented) The trimeric polypeptide complex according to claim 77, wherein amino acid residue no. 6 of exon 1 is substituted by any non-helix breaking amino acid residue, the amino acid residue numbering referring to amino acid residues in SEQ ID NO: 7.

Claim 80. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein the TTSE comprises a repeated heptad having the formula a-b-c-d-e-f-g (N to C), wherein a majority of the amino acids residues a and d are hydrophobic amino acids.

Claim 81. (Previously presented) The trimeric polypeptide complex according to claim 80, wherein the heptad is repeated 3 times and wherein the amino acid residues located at sequence positions a and d of the third occurrence of the heptad repeat are glutamine residues.

Claim 82. (Currently amended) The trimeric polypeptide complex according to claim 68 wherein the complex remains substantially as a trimer ~~at a in the~~ temperature of ~~range 50- about~~ 70°C.

Claim 83. (Previously presented) The trimeric polypeptide complex according to claim 68, comprising at least 2, 3, 4, 5 or 6 heterologous moieties.

Claim 84. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein the at least one heterologous moiety is selected from the group consisting of:

- (a) a ligand binding structure;
- (b) a toxin;
- (c) a detectable moiety;
- (d) an in situ activatable substance;
- (e) an enzyme;
- (f) a radioactive moiety;
- (g) a cytokine;
- (h) a non-proteinaceous polymer;
- (i) a polyalcohol;
- (j) a polysaccharide;
- (k) a lipid;
- (l) a polyamine;
- (m) a photo cross-linking agent; and
- (n) a group facilitating conjugation of the polypeptide to a target, wherein the conjugation encompasses both covalent and non-covalent linkages.

Claim 85. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein said at least one heterologous moiety is positioned C-terminally to the monomer polypeptide.

Claim 86. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein said at least one heterologous moiety is positioned N-terminally to the monomer polypeptide.

Claim 87. (Previously presented) The trimeric polypeptide complex according to claim 68, which comprises at least one heterologous moiety which is positioned N-terminally to at least one monomer polypeptide and at least one heterologous moiety which is positioned C-terminally to at least one monomer polypeptide.

Claim 88. (Previously presented) The trimeric polypeptide complex according to claim 68, wherein the at least one heterologous moiety is covalently linked to the monomer polypeptide via a peptide bond to the N- or C-terminus of the monomer polypeptide chain, via a peptide bond to a side chain in the monomer polypeptide, via a bond to a cysteine residue, or when more than one heterologous moiety, combinations of these locations.

Claim 89. (Previously presented) The trimeric polypeptide complex according to claim 68 which lacks any free amino and/or carboxy groups.

Claim 90. (Previously presented) A method for preparing a trimeric polypeptide complex which comprises (i) admixing three monomer polypeptides according to claim 68, (ii) effecting complex formation between said monomer polypeptides, and (iii) isolating the resulting trimeric polypeptide complex.

Claim 91. (Previously presented) A kit comprising the trimeric polypeptide complex according to claim 68.

Claim 92. (Withdrawn) A method for targeted gene therapy involving selective delivery of a material for transfection or infection of a specific population of cells, comprising the use of a trimeric polypeptide complex according to claim 68.

Claim 93. (Withdrawn) The method for targeted gene therapy according to claim 92 wherein the at least one heterologous moiety comprises a moiety selected from a ligand

binding structure such as a receptor molecule or the ligand binding part of a receptor molecule, and wherein the gene therapy involves the delivery of nucleic acids to the desired population of cells by use of a viral vector directed to cells displaying the artificial receptor complex corresponding to the heterologous moiety.

Claim 94. (Previously presented) A chimeric product comprising a trimeric polypeptide complex according to claim 68, wherein said product does not elicit an antigenic response in a human subject.

Claim 95. (Withdrawn) In a method of assembling antibody fragments into oligomeric or multivalent entities for generating chimeric artificial antibodies having preselected pharmacokinetic and/or pharmodynamic properties the improvement which comprises use of a trimeric polypeptide complex according to claim 68 as a vehicle.

Claim 96. (Withdrawn) In a method for delivering an imaging or toxin- conjugated antibody to a tumor the improvement which comprises use of a trimeric polypeptide complex according to claim 68.

Claim 97. (Withdrawn) In a method of delivering a substance to a target cell or tissue, the improvement which comprises use of a conjugate of said substance and a trimeric polypeptide complex according to claim 68.

Claim 98. (Previously presented) A composition comprising a trimeric polypeptide complex according to claim 68.

Claim 99. (Previously presented) A composition according to claim 98 wherein the trimeric polypeptide complex is comprised in a liposome.

Claim 100. (Withdrawn) A method for treating or preventing of a disease comprising administering to a subject in need thereof a therapeutically or prophylactically effective amount of a pharmaceutically acceptable composition comprising a trimeric polypeptide complex according to claim 68.

Claim 101. (Withdrawn) The method according to claim 100 wherein the composition is administered by a route selected from the group consisting of the intravenous route, the intraarterial route, the transmembraneus route of the buccal, anal or vaginal tissue, intranasal route, the pulmonary route, the transdermal route, intramuscular, subcutaneous, intratechal, inoculation into tissue, or by an implant.

Claim 102. (Previously presented) A diagnostic agent comprising a trimeric polypeptide complex according to claim 68.

Claim 103. (Previously presented) A diagnostic agent according to claim 102 wherein the at least one heterologous moiety is a detectable label.

Claim 104. (Withdrawn) A method for diagnosis of a disease comprising contacting a sample with a diagnostic agent according to claim 102, and correlating the degree of interaction between the agent and the sample, with the status of the disease.

Claim 105. (Withdrawn) In a method of displaying a protein library the improvement which comprises operably linking the library proteins to a living or nonliving support by means of a trimeric polypeptide complex according to claim 68.

Claim 106. (Previously presented) The monomer polypeptide construct of claim 1, wherein the at least one heterologous moiety is a heterologous moiety which does not exclusively facilitate expression and/or purification of the monomer polypeptide construct.

Claim 107. (Previously presented) The method according to claim 90, wherein the trimeric polypeptide complex is subjected to further processing.

Claim 108. (Previously presented) The trimeric polypeptide complex according to claim 84, wherein the ligand binding structure is selected from the group consisting of a receptor molecule, the ligand binding part of receptor molecule, an antibody, an antigen

binding antibody fragment, a molecule having antibody characteristics, a monovalent scFv antibody fragment, and a Fab antibody fragment.

Claim 109. (Previously presented) The trimeric polypeptide complex according to claim 84, wherein the toxin is ricin.

Claim 110. (Previously presented) The trimeric polypeptide complex according to claim 84, wherein the detectable label is selected from the group consisting of a fluorescence labeled molecule, a radioactively labeled molecule, and an enzymatically labeled molecule.

Claim 111. (Previously presented) The trimeric polypeptide complex according to claim 84 wherein the non-proteinaceous polymer is selected from the group consisting of a polymeric alkaloid, a polyalcohol, a polysaccharide, a lipid, and a polyamine.

Claim 112. (Previously presented) An oligomer comprising three monomer polypeptide constructs according to claim 1.

Claim 113. (Previously presented) A monomer polypeptide construct according to claim 1, wherein said TTSE is a polypeptide having at least 68% amino acid sequence identity with the consensus sequence shown in Fig. 2

Claim 114. (Previously presented) A monomer polypeptide construct according to claim 113, wherein the sequence identity with the consensus sequence is at least 81%.

Claim 115. (Previously presented) A monomer polypeptide construct according to claim 114, wherein the sequence identity with the consensus sequence is at least 87%.

Claim 116. (Previously presented) A monomer polypeptide construct according to claim 115, wherein the sequence identity with the consensus sequence is at least 92%.

Claim 117. (Previously presented) A monomer polypeptide construct according to claim 116, wherein the TTSE comprises the consensus sequence shown in Figure 2.

Claim 118. (Previously presented) A monomer polypeptide construct according to claim 1, wherein the TTSE is derived from human tetranectin, murine tetranectin, C-type lectin of bovine cartilage, or C-type lectin of shark cartilage.

Claim 119. (Previously presented) A monomer polypeptide construct according to claim 118, wherein the TTSE is derived from human tetranectin and comprises the amino acid residues V17 to V49 (exon 2) shown in Figure 1.

Claim 120. (Previously presented) A monomer polypeptide construct according to claim 119, wherein the TTSE derived from human tetranectin further comprises the amino acid residues C50 to K52 of exon 3 as shown in Figure 1.

Claim 121. (Previously presented) A monomer polypeptide construct according to claim 1, wherein the monomer polypeptide further comprises the amino acid residues E1 to D16 (exon 1) shown in Figure 1.

Claim 122. (Previously presented) A monomer polypeptide construct according to claim 119, wherein at least one amino acid residue of exon 2 selected from the group consisting of amino acid residue nos. 21, 22, 24, 25, 27, 28, 31, 32, 35, 39, 41, 42, is/are substituted by any non-helix breaking amino acid residue, the amino acid residue numbering referring to amino acid residues in SEQ ID NO:7.

Claim 123. (Previously presented) A monomer polypeptide construct according to claim 121, wherein amino acid residue no. 6 of exon 1 is substituted by any non-helix breaking amino acid residue, the amino acid residue numbering referring to amino acid residues in SEQ ID NO: 7.

Claim 124. (Previously presented) A monomer polypeptide construct according to claim 1, wherein the TTSE comprises a repeated heptad having the formula a-b-c-d-e-f-g (N to C), wherein a majority of the amino acids residues a and d are hydrophobic amino acids.

Claim 125. (Previously presented) A monomer polypeptide construct according to claim 124, wherein the heptad is repeated 3 times and wherein the amino acid residues located at sequence positions a and d of the third occurrence of the heptad repeat are glutamine residues.

Claim 126. (Previously presented) A monomer polypeptide construct according to claim 1, wherein the at least one heterologous moiety is selected from the group consisting of:

- (a) a ligand binding structure;
- (b) a toxin;
- (c) a detectable moiety;
- (d) an in situ activatable substance;
- (e) an enzyme;
- (f) a radioactive moiety;
- (g) a cytokine;
- (h) a non-proteinaceous polymer;
- (i) a photo cross-linking agent; and
- (j) a group facilitating conjugation of the polypeptide to a target, wherein the conjugation encompasses both covalent and non-covalent linkages.

Claim 127. (Previously presented) A monomer polypeptide construct according to claim 126, wherein the ligand binding structure is selected from the group consisting of a receptor molecule, the ligand binding part of receptor molecule, an antibody, an antigen binding antibody fragment, a molecule having antibody characteristics, a monovalent scFv antibody fragment, and a Fab antibody fragment.

Claim 128. (Previously presented) A monomer polypeptide construct according to claim 126, wherein the toxin is ricin.

Claim 129. (Previously presented) A monomer polypeptide construct according to claim 126, wherein the detectable label is selected from the group consisting of a

fluorescence labeled molecule, a radioactively labeled molecule, and an enzymatically labeled molecule.

Claim 130. (Previously presented) A monomer polypeptide construct according to claim 126, wherein the non-proteinaceous polymer is selected from the group consisting of a polymeric alkaloid, a polyalcohol, a polysaccharide, a lipid, and a polyamine.

Claim 131. (Previously presented) A monomer polypeptide construct according to claim 126, wherein said at least one heterologous moiety is positioned C-terminally to the monomer polypeptide.

Claim 132. (Previously presented) A monomer polypeptide construct according to claim 126, wherein said at least one heterologous moiety is positioned N-terminally to the monomer polypeptide.

Claim 133. (Previously presented) A monomer polypeptide construct according to claim 126, which comprises at least one heterologous moiety which is positioned N-terminally to the monomer polypeptide and at least one heterologous moiety which is positioned C-terminally to the monomer polypeptide.

Claim 134. (Previously presented) A monomer polypeptide construct according to claim 126, wherein the at least one heterologous moiety is covalently linked to the monomer polypeptide via a peptide bond to the N- or C-terminus of the monomer polypeptide chain, via a peptide bond to a side chain in the monomer polypeptide, via a bond to a cysteine residue, or when more than one heterologous moiety, combinations of these locations.